

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

COMMUNICATION IN CASES FOR WHICH  
NO OTHER FORM IS APPLICABLE

To:

KNOBBE, MARTENS, OLSON & BEAR, LLP  
Attn. Hart, Daniel  
2040 Main Street  
14th Floor  
Irvine, CA 92614  
UNITED STATES OF AMERICA

Date of mailing  
(day/month/year)

08/07/2005

Applicant's or agent's file reference

NEREUS.079VP

REPLY DUE

See paragraph 1 below

International application No.

PCT/US2004/019543

International filing date  
(day/month/year)

18/06/2004

Applicant

NEREUS PHARMACEUTICALS, INC.

1. ☐ REPLY DUE within \_\_\_\_\_ ~~100~~ days from the above date of mailing

☒ NO REPLY DUE

2. COMMUNICATION:

Referring to your fax of 29.06.2005, please find enclosed a corrected version of the International Search Report, that replaces and cancels the one already in your possession.

A copy of this letter has been sent to the International Bureau.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Joëlle Gerber

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:  
 KNOBBE, MARTENS, OLSON & BEAR, LLP  
 Attn. Hart, Daniel  
 2040 Main Street  
 14th Floor  
 Irvine, CA 92614  
 UNITED STATES OF AMERICA

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT AND  
 THE WRITTEN OPINION OF THE INTERNATIONAL  
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year)	08/07/2005
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Applicant's or agent's file reference NEREUS.079VP	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
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International application No. PCT/US2004/019543	International filing date (day/month/year) 18/06/2004
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Applicant NEREUS PHARMACEUTICALS, INC.	
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1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

**4. Reminders**

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
 NL-2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl  
 Fax: (+31-70) 340-3016

Authorized officer

Joëlle Gerber

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/ISA/401).

If a demand for international preliminary examination is made, the written opinion of the International Searching Authority will, except in certain cases where the International Preliminary Examining Authority did not act as International Searching Authority and where it has notified the International Bureau under Rule 66.1bis(b), be considered to be a written opinion of the International Preliminary Examining Authority. If a demand is made, the applicant may submit to the International Preliminary Examining Authority a reply to the written opinion together, where appropriate, with amendments before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later (Rule 43bis.1(c)).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the *PCT Applicant's Guide*, Volume II.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>NEREUS.079VP</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/US2004/019543</b>	International filing date (day/month/year) <b>18/06/2004</b>	(Earliest) Priority Date (day/month/year) <b>20/06/2003</b>
Applicant <b>NEREUS PHARMACEUTICALS, INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 11 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (See Box II).

3. ☒ Unity of invention is lacking (see Box III).

## 4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**USE OF [3.2.0] HETEROCYCLIC COMPOUNDS AND ANALOGS THEREOF FOR THE TREATMENT OF CANCER, INFLAMMATION AND INFECTIOUS DISEASES**

## 5. With regard to the abstract,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

## 6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2004/019543

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

Disclosed are methods of treating cancer, inflammatory conditions, and/or infectious disease in an animal comprising: administering to the animal, a therapeutically effective amount of a [3.2.0] heterocyclic compound, preferably a 6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione, such as salinosporamide A. The animal is a mammal, preferably a human or a rodent.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/019543

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-14, and 17-24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1 (partially), 2-15 (entirely), 17-20 (entirely)

Use of a compound having the structure of formula I, and pharmaceutically acceptable salts and pro-drug esters thereof in the treatment of cancer.

A method of treating a neoplastic disease in an animal, the method comprising administering to the animal a therapeutically effective amount of a compound of a formula selected from formulae I-V, and pharmaceutically acceptable salts and pro-drug esters thereof.

A pharmaceutical composition comprising a compound of a formula selected from formulae I-V, and pharmaceutically acceptable salts and pro-drug esters thereof, without an anti-microbial agent.

A method of inhibiting the growth of a cancer cell comprising contacting a cancer cell with a compound of a formula selected from formulae I-V, and pharmaceutically acceptable salts and pro-drug esters thereof.

A method of inhibiting proteasome activity or of inhibiting NF-kappaB activation comprising the step contacting a cell with a compound of a formula selected from formulae I-V, and pharmaceutically acceptable salts and pro-drug esters thereof.

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2. claims: 1 (partially), 21-22 (entirely)

Use of a compound having the structure of formula I, and pharmaceutically acceptable salts and pro-drug esters thereof in the treatment of inflammation.

A method for treating an inflammatory condition comprising administering an effective amount of a compound of a formula selected from formulae I-V to a patient in need thereof.

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3. claims: 1 (partially), 16 (entirely), 23-24 (entirely)

Use of a compound having the structure of formula I, and pharmaceutically acceptable salts and pro-drug esters thereof in the treatment of infectious disease.

A pharmaceutical composition comprising a compound of a formula selected from formulae I-V, and pharmaceutically acceptable salts and pro-drug esters thereof and an anti-microbial agent.

A method for treating a microbial illness comprising administering an effective amount of a compound of a formula selected from formulae I-V to a patient in need thereof.

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# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US2004/019543

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/407 A61P35/00 A61P35/02 A61P29/00 A61P19/02  
A61P11/06 A61P25/00 A61P17/06 A61P9/10 A61P33/00  
A61P33/02 A61P33/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, EMBASE, MEDLINE, SCISEARCH, CANCERLIT  
NAPRALERT, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	FELING ROBERT H ET AL: "Salinosporamide A: a highly cytotoxic proteasome inhibitor from a novel microbial source, a marine bacterium of the new genus salinospora." ANGEWANDTE CHEMIE (INTERNATIONAL ED. IN ENGLISH), (2003 JAN 20) 42 (3) 355-7. JOURNAL CODE: 0370543. ISSN: 0570-0833., 20 January 2003 (2003-01-20), XP002304842	1-5, 9-12,14, 15,17-20
Y	page 355, column 1, paragraph 3 - column 2, paragraph 1 page 356, column 2, paragraph 3 ----- -/-	1-3,6,8, 16,20-24

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another claim or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*I\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*B\* document member of the same patent family

Date of the actual completion of the international search

18 February 2005

Date of mailing of the international search report

- 8. 07. 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentamt 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-3040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Cielen, E

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US2004/019543

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FENICAL W. ET AL: "Marine microorganisms as a developing resource for drug discovery." PHARMACEUTICAL NEWS, 9/6 (489-494). REFS: 14 ISSN: 1071-894X CODEN: PHNEEP, 2002, XP008038137	1-3, 9-12,14, 15,17, 19,20
Y	page 493, column 1, paragraph 1  figure 4	1-3,6,8, 16,20-24
X	WO 02/47610 A (UNIV CALIFORNIA) 20 June 2002 (2002-06-20)	1-4, 9-12,14, 15,17, 19,20, 21,23
A	page 9, paragraph 2 - page 10, paragraph 1 examples 5-8,12 claims 1,3-6 figure 1	
X	[Online] XP002304843 Retrieved from the Internet: URL: <a href="http://www.newton.rcs.it/PrimoPiano/News/2003/02_Febbraio/03/Antibiotico.shtml">http://www.newton.rcs.it/PrimoPiano/News/2003/02_Febbraio/03/Antibiotico.shtml</a> [retrieved on 2003-02-02]	1-4, 9-12,14, 15,17, 19,20
A	the whole document	23
Y	GOLDBERG, ALFRED L. ET AL: "Not just research tools- proteasome inhibitors offer therapeutic promise" NATURE MEDICINE (NEW YORK, NY, UNITED STATES), 8(4), 338-340 CODEN: NAMEFI; ISSN: 1078-8956, 2002, XP008038140 page 338, column 2, paragraph 1 - column 3, paragraph 1 page 340, column 2, paragraph 2 - paragraph 3	1-3,6,8, 20-22
A	NICOLAUS B J R: "Symbiotic Approach to Drug Design" DECISION MAKING IN DRUG RESEARCH, XX, XX, 1983, pages 173-186, XP002197412	
P,X	REDDY, LELETI RAJENDER ET AL: "A Simple Stereocontrolled Synthesis of Salinosporamide A" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, 126(20), 6230-6231 CODEN: JACSAT; ISSN: 0002-7863, 22 April 2004 (2004-04-22), XP008038141	1-3, 9-12,14, 15,17, 19,20
P,Y	page 6230, column 1, paragraph 1  page 6231, column 2, paragraph 2	1-3,6,8, 16,20-24

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## INTERNATIONAL SEARCH REPORT

CORRECTED VERSION

International Application No  
PCT/US2004/019543

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	<p>WO 2004/071382 A (BAYER HEALTHCARE AG ; MAYER-BARTSCHMID ANKE (DE); MUELLER HARTWIG (DE)) 26 August 2004 (2004-08-26) page 1, paragraph 1 page 3, paragraph 2 - page 4, paragraph 2 page 6, paragraph 3 - page 12, paragraph 1 page 19, paragraph 6 - paragraph 3 examples 1-7 page 56, paragraph 4 - page 57, paragraph 1 page 58, paragraph 5 - page 60, paragraph 1 claims 1-6,8,9,11-14</p>	<p>1-5, 9-12, 14-23</p>
E	<p>US 2004/138196 A1 (FELING ROBERT H R ET AL) 15 July 2004 (2004-07-15) page 1, paragraphs 4,10-16,18 page 3, paragraphs 49-51 page 4, paragraphs 56,58 page 4, paragraph 61 - page 5, paragraph 64 claims 1-8,10-21</p>	<p>1-12, 14-20,23</p>
Y	<p>WO 96/32105 A (PRESIDENT AND FELLOWS OF HARVARD COLLEGE; SCHREIBER, STUART, L; STANDA) 17 October 1996 (1996-10-17) page 3, line 33 - page 6, line 15 page 7, line 21 - page 8, line 26 page 13, line 27 - page 14, line 12 page 81, lines 1-14 page 82, line 19 - page 83, line 2 page 84, lines 8-22 page 85, lines 3-32 page 87, lines 8-29 page 88, line 12 - page 89, line 14 page 90, line 16 - page 91, line 14 page 91, line 31 - page 92, line 4 claims 6-8,10,23,32,38,40,45-48,53-55,58</p>	<p>1-5, 9-12,14, 16-23</p>
Y	<p>WO 00/23614 A (LEUKOSITE, INC; MILLENNIUM PHARMACEUTICALS, INC) 27 April 2000 (2000-04-27) page 3, lines 3,4 page 7, lines 6-24 page 10, lines 14-23 page 11, lines 9-14</p>	<p>1,19-22</p>
Y	<p>US 2001/002391 A1 (BRAND STEPHEN ET AL) 31 May 2001 (2001-05-31) page 1, paragraph 10 page 2, paragraphs 14,25,26 page 3, paragraph 29 page 4, paragraph 51 page 5, paragraphs 74,76 claims 1-3,7,11,14,16,20</p>	<p>1,19-22</p>

-/-

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2001/051654 A1 (ELLIOTT PETER J ET AL) 13 December 2001 (2001-12-13) page 1, paragraph 3 page 2, paragraph 14-17 page 5, paragraph 76 figures scheme,1 claims 1,3-5,7,9-11 -----	1,19-22
Y	ELLIOTT, PETER J. ET AL: "The proteasome : A new target for novel drug therapies" AMERICAN JOURNAL OF CLINICAL PATHOLOGY , 116(5), 637-646 CODEN: AJCPAI; ISSN: 0002-9173, 2001, XP008007324 abstract table 1 page 638, column 2, paragraph 1 page 639, column 2, paragraph 3 page 639, column 2, paragraph 5 - page 640, column 1, paragraph 2 page 641, column 1, paragraph 1 - page 642, column 2, paragraph 4 -----	1-5, 9-12,14, 17-23
Y	CRANE, SHELDON N. ET AL: "A Novel Enantioselective Synthetic Route to Omuralide Analogues with the Potential for Species Selectivity in Proteasome Inhibition" ORGANIC LETTERS , 3(9), 1395-1397 CODEN: ORLEF7; ISSN: 1523-7060, 2001, XP008038134 page 1395, column 1, paragraph 1 - page 1396, column 2, paragraph 1 -----	1,23,24
Y	GANTT, SOREN M. ET AL: "Proteasome inhibitors block development of Plasmodium spp." ANTIMICROBIAL AGENTS AND CHEMOTHERAPY , 42(10), 2731-2738 CODEN: AMACQ; ISSN: 0066-4804, 1998, XP008038135 abstract page 2731, column 2, paragraph 2 figure 5 page 2736, column 1, paragraph 2 page 2736, column 2, paragraph 3 page 2737, column 1, paragraph 3 -----	1,23,24

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>TANG GUANGQING ET AL: "Proteasome activity is required for anthrax lethal toxin to kill macrophages" INFECTION AND IMMUNITY, vol. 67, no. 6, June 1999 (1999-06), pages 3055-3060, XP008038136 ISSN: 0019-9567 abstract page 3055, column 2, paragraph 3 figure 1 page 3056, column 2, paragraphs 2,3 page 3058, column 1, last paragraph - column 2, paragraph 1</p> <p>-----</p>	1,23,24
Y	<p>BEERS M., BERKOW R.: "The Merck Manual of Diagnosis and Therapy, seventeenth edition" 1999, MERCK RESEARCH LABORATORIES, WHITEHOUSE STATION N.J., XP002318189 page 1157, column 2, paragraph 5 - page 1158, column 2, last paragraph page 1241, column 2, paragraph 2 - page 1252, column 1, last paragraph</p> <p>-----</p>	16
E	<p>WO 2005/003137 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; FENICAL, WILLIAM, H; JENS) 13 January 2005 (2005-01-13) page 1, paragraph 3 page 2, paragraph 7 - page 7, paragraph 14 page 7, paragraph 16 - page 8, paragraph 18 page 9, paragraph 27 - page 13, paragraph 32 page 16, paragraph 49 - page 17, paragraph 51 page 19, paragraph 59 page 20, paragraph 61 - page 22, paragraph 65 example 2 claims 1,7-14</p> <p>-----</p>	1-12, 14-20,23

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/019543

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0247610	A	20-06-2002	AU 4322802 A CA 2429163 A1 EP 1341414 A2 JP 2004535766 T WO 0247610 A2 US 2003157695 A1	24-06-2002 20-06-2002 10-09-2003 02-12-2004 20-06-2002 21-08-2003
WO 2004071382	A	26-08-2004	WO 2004071382 A2	26-08-2004
US 2004138196	A1	15-07-2004	US 2004259856 A1 WO 2005003137 A1	23-12-2004 13-01-2005
WO 9632105	A	17-10-1996	US 6335358 B1 AU 705791 B2 AU 5542396 A CA 2217817 A1 EP 0820283 A1 JP 11503732 T NZ 306775 A WO 9632105 A1 US 5756764 A US 6147223 A US 6458825 B1 US 2003119887 A1 US 6214862 B1 US 6645999 B1 ZA 9602933 A	01-01-2002 03-06-1999 30-10-1996 17-10-1996 28-01-1998 30-03-1999 28-10-1999 17-10-1996 26-05-1998 14-11-2000 01-10-2002 26-06-2003 10-04-2001 11-11-2003 03-02-1997
WO 0023614	A	27-04-2000	AT 278803 T AU 762373 B2 AU 6433399 A BR 9914648 A CA 2347275 A1 CN 1331752 T DE 69920940 D1 EP 1123412 A1 JP 2002527114 T NZ 511197 A WO 0023614 A1 US 6613541 B1	15-10-2004 26-06-2003 08-05-2000 27-11-2001 27-04-2000 16-01-2002 11-11-2004 16-08-2001 27-08-2002 29-08-2003 27-04-2000 02-09-2003
US 2001002391	A1	31-05-2001	US 2003069189 A1 US 2001053760 A1 AT 240113 T AU 741802 B2 AU 6171998 A CA 2281224 A1 CN 1250376 T DE 69814618 D1 DE 69814618 T2 EP 0979096 A1 ES 2196547 T3 HK 1025266 A1 JP 2001511814 T NO 993935 A NZ 337364 A PT 979096 T WO 9835691 A1	10-04-2003 20-12-2001 15-05-2003 13-12-2001 08-09-1998 20-08-1998 12-04-2000 18-06-2003 25-03-2004 16-02-2000 16-12-2003 05-09-2003 14-08-2001 04-10-1999 29-06-2001 30-09-2003 20-08-1998

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/019543

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2001051654 A1	13-12-2001	AU 9580098 A	12-04-1999
		CA 2304622 A1	01-04-1999
		EP 1017398 A1	12-07-2000
		JP 2001517631 T	09-10-2001
		WO 9915183 A1	01-04-1999
-----			
WO 2005003137 A	13-01-2005	US 2004138196 A1	15-07-2004
		US 2004259856 A1	23-12-2004
		WO 2005003137 A1	13-01-2005
-----			